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10/521,305	01/14/2005	Toru Ishibashi	1232-5579	9351

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MORGAN & FINNEGAN, L.L.P.
3 WORLD FINANCIAL CENTER
NEW YORK, NY 10281-2101

EXAMINER	
BHAT, NARAYAN KAMESHWAR	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
10/17/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTOPatentCommunications@Morganfinnegan.com
Shopkins@Morganfinnegan.com
jmedina@Morganfinnegan.com

Office Action Summary	Application No.	Applicant(s)	
	10/521,305	ISHIBASHI ET AL.	
	Examiner	Art Unit	
	NARAYAN K. BHAT	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is written in reply to applicant's correspondence filed July 1, 2008. Claims 14 and 24 were amended.

Status of the Claims

2. The previous rejections under 35 USC §103(a) not reiterated below are withdrawn. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

3. Claims 1-24 are pending in this application.

4. Claims 1-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention there being no allowable generic or linking claim in the reply filed on March 13, 2007.

5. Claims 14 -24 are under prosecution.

Claim Objections

6. Previous objections to the claims 14 and 24 have been withdrawn in view of claim amendments.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 14-16 and 19-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iwaki et al (USPGPUB 2002/0110903 filed Dec. 13, 2001) in view of Duran et al (USPN 5,858, 653 issued Jan 12. 1999).

Regarding claims 14, 19 and 20, Iwaki et al teaches a method of immobilizing a probe to a solid phase carrier that include providing a probe molecules having an ionic group (Fig. 2, solid phase carrier -labeled as I, probe molecule -labeled by wavy line, functional group on the probe –labeled as J-, paragraph 0058 and 0059) and further teaches ionic group is mercapto group (paragraph 0023). Iwaki also teaches that probe molecules are nucleotide derivatives comprising oligonucleotides or polynucleotides (paragraph 0030) and further teaches that the DNA oligomer has thiol group, i.e., mercapto group (paragraph 0009), thus teaching a probe having a first functional group. Iwaki et al also teaches that the thiol group is incorporated into the oligonucleotide

(paragraph 0009). Instant specification defines linker as substance that exists between the probe and the first functional group and links the probe to the first functional group (instant specification, USPGPUB, paragraph 0038). Therefore, the first nucleotide that links thiol group to the oligonucleotide probe of Iwaki et al is considered the linker recited in the claim.

Iwaki et al also teaches providing a solid carrier having reactive groups X+ on the surface and further teaches reactive group comprises amino group (Fig. 2, solid phase carrier -labeled as I, reactive functional group on the surface –labeled as X+, paragraphs 0058 and 0059), thus teaching an immobilization substrate having a second functional group. Iwaki et al also teaches explicitly that the solid carrier having the first functional group J and second functional group X+ forms electrostatic bonding, i.e., ionic bonding, i.e., without covalent bonding (Fig. 2, middle panel, paragraphs 0007, 0058-0059). Teachings of Iwaki et al of first functional mercapto group on the oligonucleotide and second functional amino group on the substrate and formation of ionic bond between the probe and substrate implicitly encompasses two functional groups are directly bonded through ionic bonds. However, Iwaki et al are silent about explicitly teaching mercapto and amino functional groups are directly bonded through ionic bond.

Regarding claims 15 and 23, Iwaki et al teaches the preferred first functional group, i.e., mercapto group and the second functional group, i.e., an amino group. These are acidic and basic groups defined in the instant specification (see instant specification, USPGPUB paragraph 0036). The dissociation constant of amino group is 1.0×10^{-6} (See the instant specification, Paragraph 0025) and the mercapto group is 1.0

$x10^{-12}$ or more. The dissociation constants are inherent properties of the functional groups that are chosen and both the functional groups of the instant claim are taught by Iwaki et al. Furthermore, when the thiol group or the amino group binds to each other, causes a change in the properties that are specific to the "thiol and amino groups" including the mutual chemical shift of signals in the NMR spectrum.

Regarding claim 16, Iwaki et al teaches that probe comprises an oligonucleotide or a nucleic acid (paragraph 0030).

Regarding claim 21, Iwaki et al teaches that the second functional group is introduced by treatment of the solid phase carrier with an aminosilane coupling agent (paragraph 0076).

Regarding claim 22, Iwaki et al teaches the solid phase carrier comprises glass (paragraph 0062).

Regarding claim 24, Iwaki et al teaches a method of immobilizing a plurality of probes that are specifically bindable to a target substance to a solid phase carrier comprising the steps of providing a plurality of probe molecules having an ionic group (Fig. 2, solid phase carrier -labeled as I, a plurality of probe molecules-labeled by wavy line, functional group on the probe –labeled as J-, paragraph 0058 and 0059) and further teaches ionic group is mercapto group (paragraph 0023). Iwaki also teaches that probe molecules are nucleotide derivatives comprising oligonucleotides or polynucleotides (paragraph 0030) and further teaches that the DNA oligomer has thiol group, i.e., mercapto group (paragraph 0009), thus teaching a probe having a first functional group. Iwaki et al also teaches that the thiol group is incorporated into the

oligonucleotide (paragraph 0009). The first nucleotide that links thiol group to the oligonucleotide probe of Iwaki et al is the linker of the claim.

Iwaki et al also teaches providing a solid carrier having a plurality of reactive groups X+ on the surface and further teaches reactive group comprises amino group (Fig. 2, solid phase carrier -labeled as I, a plurality of reactive functional group on the surface –labeled as X+, Fig. 5, Example 3 paragraphs 0058-0059 and 0127-0142), thus teaching an immobilization substrate having a plurality of second functional groups. Iwaki et al also teaches explicitly that the solid carrier having the first functional group J and second functional group X+ forms electrostatic bonding, i.e., ionic bonding, i.e., without covalent bonding (Fig. 2, middle panel, paragraphs 0007, 0058-0059). Teachings of Iwaki et al of first functional mercapto group on the oligonucleotide and second functional amino group on the substrate and formation of ionic bond between the probe and substrate implicitly encompasses two functional groups are directly bonded through ionic bonds.

Regarding claims 14 and 24, Iwaki et al are silent about explicitly teaching mercapto and amino functional groups are directly bonded through ionic bond. However, ionic binding between mercapto and amino functional groups was known in the art at the time of the claimed invention was made as taught by Duran et al.

Duran et al teaches a method of attaching reagents to substrate comprising attaching amine functional groups to the surface and binding oligonucleotides comprising sulfhydryl groups, i.e., mercapto groups by electrostatic bonding (i.e., ionic

bonding), thus teaching explicitly direct binding of mercapto group and the amino group are directly bonded through ionic bond (column 3, lines 21-33).

Duran et al also teaches electrostatic attraction enhances the ability of the reactive groups on the surface to efficiently couple with corresponding reactive groups on the nucleic acid sequences (column 3, lines 25-28) to increase the coating efficiency of probe molecules on the surface.

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the implicit teaching of ionic bonding between mercapto and amino functional groups of Iwaki et al with explicit teaching of ionic bonding between mercapto and amino functional groups of Duran et al with a reasonable expectation of success.

An artisan would have been motivated to modify the implicit teaching of ionic bonding between mercapto and amino functional groups of Iwaki et al with explicit teaching of ionic bonding between mercapto and amino functional groups of Duran et al with the expected benefit of enhancing the interaction between functional groups for efficient coupling of thiolated nucleic acid sequences to the surface to increase the probe concentration on the surface to increase the sensitivity of target detection as taught by Duran et al (column 3, lines 25-28).

10. Claims 14, 16, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iwaki et al (USPGPUB 2002/0110903 filed Dec. 13, 2001) in view of

Duran et al (USPN 5,858, 653 issued Jan 12. 1999) as applied to claim 14 above, and further in view of McGovern et al (USPN 6,159,695 issued December 12, 2000).

Claim 17 is dependent from claim 16. Claims 16 and 18 are dependent from claim 14. Teachings of Iwaki et al and Duran et al regarding the claims 14 and 16 are described previously in this office action in section 8.

Regarding claims 17 and 18, Iwaki et al teaches that a SH- reactive group is incorporated into the oligonucleotide (paragraph 0009). In the instant specification linker is described as substance that exists between the probe and the first functional group and links the probe to the first functional group (instant specification, USPGPUB, paragraph 0038). Teaching of Iwaki et al of first nucleotide that links thiol group to the oligonucleotide, thus is the linker of the claim. Iwaki et al and Duran et al are silent about the location of the linker and linker comprising polyether chain. However, location of the linker and linker comprising polyether chain was known in the art at the time of the claimed invention was made as taught by McGovern et al.

McGovern et al teaches attachment of tether linker to oligonucleotides to introduce sulfhydryl group at the 3' end (Fig. 4A and column 15, lines 16-20) and linker comprise polyether linker of 2-50 unit (column 22, lines 53 –58). McGovern et al also teaches tether linker supply the oligonucleotide with reactive functionality so that it can be chemically manipulated, and to allow the oligonucleotide to extend any specified distance away from the surface (column 7, lines 18-22).

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the linker of Iwaki et al and Duran et al with the polyether linker of McGovern et al with a reasonable expectation of success.

An artisan would be motivated to modify the linker of Iwaki et al and Duran et al with the polyether linker of McGovern et al with the expected benefit of providing additional reactive functionality so that probe can be chemically manipulated, thus allowing the oligonucleotide to extend any specified distance away from the surface as taught by McGovern et al (column 7, lines 18-22).

Response to remarks from the Applicants

Claim Rejections under 35 U.S.C. § 103(a)

11. Applicant's arguments with respect to claims 14-17 and 19-24 being unpatentable over Chrissey et al, Iwaki et al and Meisenburg et al have been fully considered but are moot in view of the withdrawal of the rejection and new grounds of rejection set forth in this office action (Remarks, pgs. 6-10). Applicants arguments with respect to teachings of Iwaki et al as it pertains to the rejection set forth in this office action are addressed below.

Applicants argue that “Iwaki et al teaches electrostatic interaction between phosphodiester backbone of the oligomeric DNA and amino group of the organosilane and not between the mercapto group on the DNA oligomer and the amino group on the organosilane” (Remarks, pg. 8, paragraph 2). This argument is not persuasive for the following reasons. Claims 14-16, 19-23 and 24 have been rejected over Iwaki et al in

view of Duran et al under 35 USC 103(a) and not under 35USC 102 (b). As described in this office action in section 8, Iwaki et al teaches probe nucleic acid molecules comprising mercapto group and surface comprising amino group are bonded together by electrostatic bonding, i.e., ionic bonding (Fig. 2, paragraphs 0009, 0023, 0059). Duran et al explicitly teaches direct ionic bonding between mercapto group and surface comprising amino group (Office action, section 8, Duran et al, column 3, lines 21-33). Since Iwaki et al and Duran et al teaches all the recited steps of claims 14 and 24, Applicants arguments are not persuasive.

Applicant argues that "Iwaki et al teaches that electrostatic interaction requires a thickening agent, otherwise the retention ratio after washing is very low" (Remarks, pg. 8, last paragraph, pg. 9, first paragraph). This argument is not persuasive because Applicants arguments are not related to the electrostatic binding of probe molecules rather it is related to another embodiment (i.e., covalent bonding). Applicant's argument regarding the retention ratio is not persuasive because Applicants have misconstrued the teachings of evaluation of different blocking agents in the hybridization reaction to the retention ratio of the probes on the surface (see paragraph 0110).

Applicants argue that "Iwaki explicitly discloses covalent bonding between surface amino group and mercapto group of oligonucleotide synthesized and thus clearly lead away from the claimed invention" (Remarks, pg. 9, paragraph 2). This argument is not persuasive because Iwaki et al teaches two different embodiments, covalent bonding of nucleic acid probes using non-ionic reactive groups (Fig. 1, paragraphs 0017-0042, Examples 1 and 2) and electrostatic binding of probes (Fig. 2,

paragraphs 0057- 0061, Example 3). Iwaki et al teaches ionic bonding between mercapto and amino groups implicitly. Furthermore, as described above, Duran et al teaches ionic bonding between mercapto and amino groups explicitly (office action section 8, Duran et al column 3, and lines 21-33).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, Applicants argue that "Iwaki et al explicitly disclose oligonucleotide probe with mercapto group and surface with amino groups to be used for covalent bonding" (Remarks, pg. 9, paragraph 2). This argument is not persuasive because of the following reasons.

Claims 14-16, 19-23 and 24 have been rejected over Iwaki et al in view of Duran et al under 35 USC 103(a) and not under 35USC 102 (b). Iwaki et al teaches two different embodiments, covalent bonding of nucleic acid probes using non-ionic reactive groups (Fig. 1, paragraphs 0017-0042, Examples 1 and 2) and electrostatic binding of probes (Fig. 2, paragraphs 0057- 0061, Example 3). Iwaki et al teaches ionic bonding between mercapto and amino groups implicitly and Duran et al teaches ionic bonding between mercapto and amino groups explicitly (office action section 8, column 3, lines 21-33).

Applicants argue that "Meisenburg et al of teaching of mercapto group is an anionic group requires undue experimentation" (Remarks, pg. 9, last paragraph, pg. 10,

first paragraph). This argument is moot in view of the withdrawal of the rejection and new grounds of rejection set forth in this office action.

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Narayan K. Bhat whose telephone number is (571)-272-5540. The examiner can normally be reached on 8.30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla can be reached on (571)-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Narayan K. Bhat/

Examiner, Art Unit 1634

Narayan K. Bhat, Ph. D.

/Ram R. Shukla/

Supervisory Patent Examiner, Art Unit 1634